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data from INPADOC
NEWS 4 FEB 28 BABS - Current-awareness alerts (SDIs) available
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               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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L1        57667 SRC
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=> s (Pas domain) (4A) Binding
L2          142 (PAS DOMAIN) (4A) BINDING

=> s (Pas domain) (4A) hydrophobic
L3            2 (PAS DOMAIN) (4A) HYDROPHOBIC

=> s (Pas domain) (4A) hydrophobic or core or nucleus or center
L4      2435166 (PAS DOMAIN) (4A) HYDROPHOBIC OR CORE OR NUCLEUS OR
CENTER

=> s (Pas (w) domain) (4A) (hydrophobic or core or nucleus or center)
   3 FILES SEARCHED...
L5            7 (PAS (W) DOMAIN) (4A) (HYDROPHOBIC OR CORE OR NUCLEUS
OR CENTER)


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L6            2 L2 AND L5

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L7            2 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> d l7 1-2 bib ab

L7   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2005:303296  CAPLUS
DN   142:351757
TI   Foreign PAS ligands regulate PAS domain function
IN   Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.;
Card, Paul B.;
     Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight,
Steven L.
PA   Board of Regents, the University of Texas System, USA
SO   U.S. Pat. Appl. Publ., 18 pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.
DATE
     ---------------     ----   --------    --------------------
--------
PI   US 2005074846        A1    20050407    US 2003-677734
20031001
     WO 2005033662        A2    20050414    WO 2004-US32417
20041001
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
PRAI US 2003-677734 A 20031001
AB Specific binding of a foreign **core** ligand to a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first NMR spectrum of the PAS domain in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second NMR spectrum of the PAS domain in the absence of the ligand to infer the presence the ligand specifically bound within the **hydrophobic core** of the **PAS domain**. A functional surface **binding** specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the **hydrophobic core** of the **PAS domain** a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface **binding** specificity of the **PAS domain**.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:513152 CAPLUS
DN 141:50134
TI NMR detection of foreign PAS domain ligands
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.
PA Board of Regents, University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003 59,917.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004121409	A1	20040624	US 2003-677733	20031001
	US 6319679	B1	20011120	US 2001-770170	20010126
	US 2003059917	A1	20030327	US 2001-59962	20011119
PRAI	US 2001-770170	A3	20010126		
	US 2001-59962	A2	20011119		

AB Specific binding of a foreign **core** ligand to a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first NMR spectrum of the PAS domain in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second NMR spectrum of the PAS domain in the absence of the ligand to infer the presence the ligand specifically bound within the **hydrophobic core** of the **PAS domain**. A functional surface **binding** specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and, comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the **hydrophobic core** of the **PAS domain** a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface **binding** specificity of the **PAS domain**.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	47.61	47.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.46	-1.46

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LAST RELOADED: Jun 17, 2005 (20050617/UP).

=> d l4 1-2 bib ab
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L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:303296 CAPLUS
DN 142:351757
TI Foreign PAS ligands regulate PAS domain function
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.; Card, Paul B.;
Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight, Steven L.
PA Board of Regents, the University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005074846	A1	20050407	US 2003-677734	20031001
WO 2005033662	A2	20050414	WO 2004-US32417	20041001

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-677734 A 20031001
AB Specific binding of a foreign core ligand to a PAS domain, wherein the PAS

domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first **NMR** spectrum of the **PAS domain** in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second **NMR** spectrum of the **PAS domain** in the absence of the ligand to infer the presence the ligand specifically bound within the hydrophobic core of the PAS domain. A functional surface **binding** specificity of a **PAS domain**, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the hydrophobic core of the PAS domain a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface **binding** specificity of the **PAS domain**.

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:513152 CAPLUS
DN 141:50134
TI **NMR** detection of foreign **PAS domain** ligands
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.
PA Board of Regents, University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003 59,917.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004121409	A1	20040624	US 2003-677733	20031001
US 6319679	B1	20011120	US 2001-770170	20010126
US 2003059917	A1	20030327	US 2001-59962	20011119

PRAI US 2001-770170 A3 20010126
US 2001-59962 A2 20011119
AB Specific binding of a foreign core ligand to a PAS domain, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity,

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	26.92

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-2.19

FILE 'STNGUIDE' ENTERED AT 12:02:42 ON 24 JUN 2005

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 17, 2005 (20050617/UP).

=>

=> d l5 1-7 bib ab

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:303296 CAPLUS
DN 142:351757
TI Foreign PAS ligands regulate PAS domain function
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. a.; Card, Paul B.;
Harper, Shannon; Rutter, Jared; Bruick, Richard K.; McKnight, Steven L.
PA Board of Regents, the University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005074846	A1	20050407	US 2003-677734	20031001
WO 2005033662	A2	20050414	WO 2004-US32417	20041001

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-677734 A 20031001
AB Specific binding of a foreign core ligand to a PAS domain, wherein the PAS
domain is predetd., prefolded in its native state, and comprises a
hydrophobic core that has no NMR-apparent a priori formed ligand cavity,

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L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:513152 CAPLUS
DN 141:50134
TI **NMR** detection of foreign **PAS domain** ligands
IN Gardner, Kevin H.; Amezcua, Carlos A.; Erbel, Paulus J. A.; Card, Paul B.
PA Board of Regents, University of Texas System, USA
SO U.S. Pat. Appl. Publ., 18 pp., Cont.-in-part of U.S. Pat. Appl. 2003 59,917.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004121409	A1	20040624	US 2003-677733	20031001
US 6319679	B1	20011120	US 2001-770170	20010126
US 2003059917	A1	20030327	US 2001-59962	20011119

PRAI US 2001-770170 A3 20010126
US 2001-59962 A2 20011119
AB Specific binding of a foreign core ligand to a PAS domain, wherein the PAS domain is predetd., prefolded in its native state, and comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is determined by (a) detecting a first **NMR** spectrum of the

PAS domain in the presence of a foreign ligand; and (b) comparing the first NMR spectrum with a second **NMR** spectrum of the **PAS domain** in the absence of the ligand to infer the presence the ligand specifically bound within the hydrophobic core of the PAS domain. A functional surface binding specificity of a PAS domain, wherein the PAS domain is predetd., prefolded in its native state, and, comprises a hydrophobic core that has no NMR-apparent a priori formed ligand cavity, is changed by (a) introducing into the hydrophobic core of the PAS domain a foreign ligand of the PAS domain; and (b) detecting a change in the functional surface binding specificity of the PAS domain.

L5 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 1
AN 2004119294 MEDLINE
DN PubMed ID: 15009198
TI The PAS fold. A redefinition of the PAS domain based upon structural prediction.
AU Hefti Marco H; Francoijs Kees-Jan; de Vries Sacco C; Dixon Ray; Vervoort Jacques
CS Laboratory of Biochemistry, Wageningen University, the Netherlands..
marco@keydp.com
SO European journal of biochemistry / FEBS, (2004 Mar) 271 (6) 1198-208.
Journal code: 0107600. ISSN: 0014-2956.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040311
Last Updated on STN: 20040428
Entered Medline: 20040427
AB In the postgenomic era it is essential that protein sequences are annotated correctly in order to help in the assignment of their putative functions. Over 1300 proteins in current protein sequence databases are predicted to contain a PAS domain based upon amino acid sequence alignments. One of the problems with the current annotation of the PAS domain is that this domain exhibits limited similarity at the amino acid sequence level. It is therefore essential, when using proteins with

low-sequence similarities, to apply profile hidden Markov model searches
for the PAS domain-containing proteins, as for the PFAM database. From
recent 3D X-ray and **NMR** structures, however, **PAS domains** appear to have a conserved 3D fold as shown here by
structural alignment of the six representative 3D-structures from the PDB
database. Large-scale modelling of the PAS sequences from the PFAM
database against the 3D-structures of these six structural prototypes was
performed. All 3D models generated (> 5700) were evaluated using prosaii.
We conclude from our large-scale modelling studies that the PAS and PAC
motifs (which are separately defined in the PFAM database) are directly
linked and that these two motifs form the PAS fold. The existing
subdivision in PAS and PAC motifs, as used by the PFAM and SMART
databases, appears to be caused by major differences in sequences in the
region connecting these two motifs. This region, as has been shown by
Gardner and coworkers for human PAS kinase (Amezcua, C.A., Harper, S.M.,
Rutter, J. & Gardner, K.H. (2002) Structure 10, 1349-1361, [1]), is very
flexible and adopts different conformations depending on the bound ligand.
Some PAS sequences present in the PFAM database did not produce a good
structural model, even after realignment using a structure-based alignment
method, suggesting that these representatives are unlikely to have a fold
resembling any of the structural prototypes of the PAS domain superfamily.

L5 ANSWER 4 OF 7 CABA COPYRIGHT 2005 CABI on STN
AN 2003:130562 CABA
DN 20033102640
TI The NifL PAS domain - insight into its structure and function
AU Hefti, M. H.
CS Wageningen University, Postbus 9101 6700 HB Wageningen, Netherlands.
SO The NifL PAS domain: insight into its structure and function, (2003) pp.
115. 332 ref.
Publisher: Wageningen Universiteit (Wageningen University). Wageningen
ISBN: 90-5808-809-X

CY Netherlands Antilles
DT Dissertation
LA English
SL Dutch
ED Entered STN: 20030812
Last Updated on STN: 20030812
AB This thesis contains 8 chapters focusing on the PAS domain of the nitrogen fixation regulatory protein NifL from Azotobacter vinelandii. PAS domains are found in sensor proteins and are named after homology between the Drosophila period protein (PER), the aryl hydrocarbon receptor nuclear translocator protein (ARNT) and the Drosophila single-minded protein (SIM). The first chapter provides a brief review on nitrogen fixation and the biochemical importance of PAS domains. The NifL protein is a flavoprotein, with flavin adenine dinucleotide (FAD) as the prostethic group. The second chapter summarizes the tools currently available within the field of flavoprotein deflavination and reconstitution. A new purification method for Histidine-tagged proteins is described in the next chapter. On-column cleavage of the protein with thrombin facilitates the separation of the protein of interest and the His-tag. In chapter 4, the His-tag is again used as a tool to deflavinate and reconstitute the NifL PAS domain protein. Chapter 5 describes the current status of the structure elucidation of this domain, using X ray crystallography. Small-angle X ray scattering (SAXS) studies with this domain clearly showed the tetrametric state of the PAS domain. In an envelope, created using SAXS data, four monomeric models of the PAS domain were fitted to elucidate the structural arrangement of these four monomers (chapter 6). In the next chapter, the term PAS fold is introduced to denote a three-dimensional fold present in several proteins. The 3D structures determined of a PAS domain containing protein include: (i) the structure of the Ectothiorhodospira halophila blue-light receptor photoactive yellow protein; (ii) structure of the heme-binding domain of the rhizobial oxygen

sensor FixL from Bradyrhizobium japonicum and from Rhizobium meliloti; and
(iii) the N-terminal domain of the human ether-a-go-go-related potassium
channel HERG, the flavin mononucleotide containing phototropin module of
the chimeric fern Adiantum photoreceptor, and the average **NMR** structure of the N-terminal **PAS domain** of human PAS
kinase. Some concluding remarks are provided in the final chapter.

L5 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 2
AN 2003611132 MEDLINE
DN PubMed ID: 14668441
TI Structural basis for PAS domain heterodimerization in the basic helix--loop--helix-PAS transcription factor hypoxia-inducible factor.
AU Erbel Paul J A; Card Paul B; Karakuzu Ozgur; Bruick Richard K; Gardner
Kevin H
CS Departments of Biochemistry and Pharmacology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390,
USA.
NC CA90601 (NCI)
CA95471 (NCI)
GM08297 (NIGMS)
SO Proceedings of the National Academy of Sciences of the United States of
America, (2003 Dec 23) 100 (26) 15504-9. Electronic Publication: 2003-12-10.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20031225
Last Updated on STN: 20040421
Entered Medline: 20040420
AB Biological responses to oxygen availability play important roles in
development, physiological homeostasis, and many disease processes. In
mammalian cells, this adaptation is mediated in part by a conserved
pathway centered on the hypoxia-inducible factor (HIF). HIF is a heterodimeric protein complex composed of two members of the basic
helix-loop-helix Per-ARNT-Sim (PAS) (ARNT, aryl hydrocarbon receptor
nuclear translocator) domain family of transcriptional activators,

HIFalpha and ARNT. Although this complex involves protein-protein interactions mediated by basic helix-loop-helix and PAS domains in both proteins, the role played by the PAS domains is poorly understood. To address this issue, we have studied the structure and interactions of the C-terminal **PAS domain** of human HIF-2alpha by **NMR** spectroscopy. We demonstrate that HIF-2alpha PAS-B binds the analogous ARNT domain in vitro, showing that residues involved in this interaction are located on the solvent-exposed side of the HIF-2alpha central beta-sheet. Mutating residues at this surface not only disrupts the interaction between isolated PAS domains in vitro but also interferes with the ability of full-length HIF to respond to hypoxia in living cells. Extending our findings to other PAS domains, we find that this beta-sheet interface is widely used for both intra- and intermolecular interactions, suggesting a basis of specificity and regulation of many types of PAS-containing signaling proteins.

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:729661 CAPLUS
DN 139:303399
TI Structural basis of a phototropin light switch
AU Harper, Shannon M.; Neil, Lori C.; Gardner, Kevin H.
CS Departments Biochemistry and Pharmacology, Univ. Texas Southwestern Medical Center, Dallas, TX, 75390-9038, USA
SO Science (Washington, DC, United States) (2003), 301(5639), 1541-1544
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB Phototropins are light-activated kinases important for plant responses to blue light. Light initiates signaling in these proteins by generating a covalent protein-FMN adduct within sensory Per-ARNT-Sim (PAS) domains. We characterized the light-dependent changes of a phototropin **PAS domain** by solution **NMR** spectroscopy and found that an α helix located outside the canonical domain plays a key role in this activation process. Although this helix assocs. with the PAS core in

the dark, photoinduced changes in the domain structure disrupt this
interaction. We propose that this mechanism couples light-dependent bond
formation to kinase activation and identifies a signaling pathway
conserved among PAS domains.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 3
AN 2002619803 MEDLINE
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TI Structure and interactions of PAS kinase N-terminal PAS domain: model for
intramolecular kinase regulation.
CM Comment in: Chem Biol. 2002 Nov;9(11):1165-6. PubMed ID: 12445766
AU Amezcua Carlos A; Harper Shannon M; Rutter Jared; Gardner Kevin H
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SO Structure (Cambridge, Mass. : 2001), (2002 Oct) 10 (10) 1349-61.

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AB PAS domains are sensory modules in signal-transducing proteins that
control responses to various environmental stimuli. To examine how those
domains can regulate a eukaryotic kinase, we have studied the structure
and binding interactions of the N-terminal **PAS domain**
of human PAS kinase using solution **NMR** methods. While this
domain adopts a characteristic PAS fold, two regions are unusually
flexible in solution. One of these serves as a portal that allows small
organic compounds to enter into the core of the domain, while the other
binds and inhibits the kinase domain within the same protein. Structural
and functional analyses of point mutants demonstrate that the compound and
ligand binding regions are linked, suggesting that the PAS domain serves

as a ligand-regulated switch for this eukaryotic signaling system.

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